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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/830,195	BUISER ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-17,19-31,49-54 and 56-59* is/are pending in the application.

4a) Of the above claim(s) *16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-4,6-15,17,19-31,49-54 and 56-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 11/24/2008, in reply to the Office Action mailed 10/09/08, is acknowledged and has been entered. Claims 1 and 54 have been amended. Claims 1-4, 6-17, 19-31, 49-54 and 56-59 are pending and are examined herein on the merits for patentability.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/22/2008 has been entered.

Response to Arguments

Applicant's arguments filed 11/24/2008 have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 8, 9, 15, 17, 19 – 23, 25, 26, 28 – 31, 49 – 54 and 56 – 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobsen (US 6,530,943) and Greene (US 2002/0177855), in view of Smith *et al.* (US 5,888,930).

Jacobsen discloses an embolic device comprised of a linear sequence of flexibly interconnected miniature beads. The device generally comprises a flexible elongated filament having a linear sequence of beads disposed thereon. The beads may be fixedly connected to the filament. The string of beads may be configured to the exact length needed. The beads may be porous (abstract). The embolic device is used to occlude blood flow and/or initiate blood clotting upon introduction to the body via a catheter (column 1, lines 14 – 25). The string of beads includes a filament (i.e. a link) and beads. The beads have diameters from 0.002 inches to 0.0018 inches, and may be made of a variety of materials, including polymers, radioopaque polymers, metals. The string of beads may be comprised of beads of several different materials (column 4, lines 25 – 40). The filament can be a multi or monofilament polymer (column 5, line 21). The string of beads may be configured as a drug delivery device, wherein the beads are porous and contain a medicament for controlled release into the interior of the body (column 2, lines 44 – 47), as set forth above.

Greene discloses an embolization device for occluding a body cavity which includes one or more elongated hydrophilic embolizing elements non-releasably carried along the length of an elongated filamentous carrier (abstract). The embolizing agents (micropellets) may be made of a macroporous polymeric material or a porous, environmentally-sensitive, expansile hydrogel (abstract and paragraphs 0085 – 0088). The carrier (i.e. link) is preferably a nickel/titanium wire, but may also be formed from a polymer (paragraph 0093). The carrier has a diameter of approximately 0.04 mm (i.e. 0.0015 inches) (paragraph 0092). The length of the carrier is variable depending on the size of the vascular site to be embolized (paragraph 0085). See also Figure 1. The device may be contained in saline solution (paragraph 0029). The devices may be used to deliver therapeutic agents (paragraph 0141).

Jacobsen and Greene do not specifically recite that the porous beads have an interior and surface regions with a density of large pores, wherein the density of pores of the interior region is greater than that of the surface region.

Smith discloses polymeric microporous beads having an anisotropic pore structure of large pores in the interior and smaller pores at the surface, the gradation of pore sizes between the interior and surface being continuous (abstract). It is noted that the instantly claimed particles do not prohibit the size of the interior pores being larger than that of the surface pores. It is interpreted that the particles of Smith demonstrate a larger pore density on the interior of the particle than on the surface, and accordingly that the particles of Smith are within the scope of those claimed (see Figure 1). The pores can be loaded with an active ingredient, and the particles are used as controlled-

release of an active agent (column 1 – 2). The particles are generally spherical in shape, with diameters ranging from about 5 microns to about 5 mm (column 2, line 49).

Smith fails to teach particles which are connected.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize the porous particles having a pore size distribution as disclosed by Smith as the porous beads in the embolic device comprised of a linear sequence of flexibly interconnected miniature beads, taught by Jacobsen, or the embolic micropellets positioned along the length of a carrier, taught by Greene, because the embolic devices of Jacobsen or Greene and the particles of Smith are used for controlled release drug delivery (see Jacobsen column 2, lines 44 – 47). One would have been motivated to do so because Smith specifically teaches that microporous beads having an asymmetric pore structure are particularly useful for delivery of active agents for an extended period of time (see Smith, column 2, lines 15 – 30). Regarding claims 3, 4, 6, 7 and 49 – 53, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges. Regarding claim 56, Greene teaches a particularly desirable porous polymeric material to be PVA (column 11, lines 55+). Regarding the limitations wherein the particle chain includes at least one of the following: (a) the link having an aspect ratio of at most about 1000 **or** the link having an aspect ratio of about 0.001; and (b) a ratio of the diameter of one of the at least two particles to a width of the link is at least about 0.5 **or** the ratio of the diameter of one of the at least two particles to a width of the link is at most about 100, it is respectfully

noted that *any* number would read on the instantly claimed aspect ratios when stated in the alternative. For example, with regard to the link a number such as 1001 is greater than 1000, and thus would not read on "at most 1000," but reads on "at least 0.001." Likewise, with regard to diameter of particle to width of link, a number such as 0.1 is less than 0.5 and thus would not read on "at least 0.5," but reads on "at most about 100." Furthermore, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio within the extremely broad ranges based on the diameter of the particles as a ratio to any length available.

Applicant argues on pages 8-11 of the Response that Jacobsen and Greene describe chains of joined beads (Jacobsen, e.g., col. 2, lines 35-38) or embolizing elements along a filament (Greene, e.g., paragraph [0016]). Applicant asserts that Jacobsen emphasizes the importance of joining beads having a "central bore," and formed of a material having a particular density and surface porosity (Jacobsen, e.g., col. 4, lines 28-53). The joined embolizing elements described in Greene are formed from a polymer with sufficient softness to be "coaxially skewered" along a carrier filament, or the embolizing elements are molded around the carrier filament (Greene, e.g., paragraphs [0016] and [0021] - [0024]). Smith describes porous beads having very specific pore structures formed by precipitation methods that require certain specific combinations of solvents, non-solvent liquids and polymers (e.g., Smith at col. 3, lines

6-67; col. 5, lines 13-27). Applicant asserts that Smith notably fails to disclose how to form such particles having the "central bore" and density requirements emphasized by Jacobsen, or the softness to permit "coaxial skewering" along a filament in the manner disclosed in Greene. Applicant argues that the Office Action points to no basis for modifying the teachings of the porous particles in Smith to arrive at the claimed composition of connected particles, and that the cited references, alone or in combination, do not disclose or render obvious joining the beads of Smith according to the teachings of Greene or Jacobsen, nor do Greene or Jacobsen disclose or render obvious the modification of the particles produced in Smith to obtain the claimed compositions. Applicant further argues that the obviousness rejection is improper because the asserted combination of Jacobsen, Smith and Greene do not enable the claimed particle chains having a particle with a mean pore size in an interior region greater than the mean pore size in a surface region, and that applicable caselaw clearly states that "[i]n order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." *Beakman Instruments, Inc. v. LKBProdukterAB,* 892 F2d 1547, 1551, 13 USPQ2d 1301, 1304 (Fed. Cir. 1989). A claim rejection for obviousness under 35 USC 103 is improper if the person of ordinary skill in the art would not be able to make a claimed composition or perform a claimed method upon reviewing the cited prior art without undue experimentation. Applicant asserts that undue experimentation would be required to make and use the claimed connected particles based on the asserted combination of Jacobsen, Smith and Greene.

This is not found to be persuasive. With regard to Applicant's argument that Jacobsen emphasizes the importance of joining beads having a central bore and formed of a material having a particular density and surface porosity, Jacobsen clearly teaches that his particles can have a density which is less than that of blood (e.g. approximately 1060 kg/m^3) (column 4, line 30-31), or a density which is greater than that of blood (column 4, line 33). Therefore, Jacobsen clearly teaches a range of densities to be desirable (e.g. less than or greater than that of blood), and that density can be varied to suit a desired function. Regarding the porosity of the particles, Jacobsen does not recite any specific surface porosity, as alleged by Applicant and Smith clearly teaches porous particles. Applicant has provided no evidence to support that the properties of the particles of Smith would make them unsuitable for use as beads in the device of Johnson. Regarding the presence of a central bore, one of ordinary skill would be capable of providing such a feature, e.g. such as by skewering as taught by Greene. Applicant argues that Greene teaches a polymer with sufficient softness to be "coaxially skewered" along a carrier filament, or the embolizing elements are molded around the carrier filament, however, has not provided evidence to support that the materials of Smith would be incapable of such properties, e.g. softness. Therefore, the disclosures of Jacobsen and Greene describing various preparatory methods would not require undue experimentation for the skilled artisan. It is further noted that the instant claims are composition claims, not method of making claims. Furthermore, see MPEP 2145 (III) regarding arguing that prior art devices are not physically combinable. "The test for obviousness is not whether the features of a

secondary reference may be bodily incorporated into the structure of the primary reference.... Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). See also *In re Sneed*, 710 F.2d 1544, 1550, 218 USPQ 385, 389 (Fed. Cir. 1983) ("[I]t is not necessary that the inventions of the references be physically combinable to render obvious the invention under review."); and *In re Nievelt*, 482 F.2d 965, 179 USPQ 224, 226 (CCPA 1973) ("Combining the teachings of references does not involve an ability to combine their specific structures.").

Claims 1 – 4, 6 – 15, 17, 19 – 26, 28 – 31, 49 – 54 and 56 – 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobsen (US 6,530,943) and Greene (US 2002/0177855), in view of Smith *et al.* (US 5,888,930), in further view of Mazzocchi (US 6,605,102).

Jacobsen discloses an embolic device comprised of a linear sequence of flexibly interconnected miniature beads. The beads are porous and contain a medicament for controlled release into the interior of the body, as set forth above.

Greene discloses an embolization device for occluding a body cavity which includes one or more elongated, hydrophilic embolizing elements non-releasably carried along the length of an elongated filamentous carrier, as set forth above.

Jacobsen and Greene do not specifically recite that the porous beads have an interior and surface regions with a density of large pores, wherein the density of pores

of the interior region is greater than that of the surface region. Jacobsen and Green also fail to specifically recite the length of the particle chain or the aspect ratio.

Smith discloses polymeric microporous beads having an anisotropic pore structure of large pores in the interior and smaller pores at the surface, the gradation of pore sizes between the interior and surface being continuous. The beads may vary in diameter from about 5 microns to about 5 mm, as set forth above, thus it is interpreted that a variety of sizes of particles may be used.

Smith fails to teach particles which are connected.

Mazzocchi teaches embolic devices which may have a variety of structures (abstract). The aspect ratio of the device ranges from about 1.0 to about 3.0, where an aspect ratio of 2.0 is preferred (column 11, lines 59+). The length of the devices may vary, but may be for example 25 mm (column 12, line 62). Mazzocchi does not teach that the embolic device is a particle chain.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize the porous particles of Smith as the porous beads in the embolic device comprised of a linear sequence of flexibly interconnected miniature beads, taught by Jacobsen, or the embolic micropellets positioned along the length of a carrier, taught by Greene, because both the embolic devices of Jacobsen or Greene and the particles of Smith are used for controlled release drug delivery (see Jacobsen column 2, lines 44 – 47). One would have been motivated to do so because Smith specifically teaches that asymmetric microporous beads control the release of an agent from the particle, and are particularly useful for delivery of desired drug dosages for an

extended period of time (see Smith, column 1 – 2). Regarding the specific dimensions of the devices, Greene also teaches an elongated carrier with embolic agents (micropellets) attached thereto, and teaches the width of the carrier (i.e. chain or link) to be within the claimed range, and also teaches that the length of the carrier can be varied depending on the vascular site to be embolized (column 11, line 20), and accordingly it would have been obvious to utilize chain with a variety of lengths (i.e. thereby effecting the aspect ratio), especially because Mazzocchi further shows that embolic devices are generally known in the art to have length / width / aspect ratio dimensions within the claimed ranges. Regarding claims 3, 4, 6, 7 and 49 – 53, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges. Regarding claim 56, Greene teaches a particularly desirable porous polymeric material to be PVA (column 11, lines 55+). Regarding the limitations wherein the particle chain includes at least one of the following: (a) the link having an aspect ratio of at most about 1000 **or** the link having an aspect ratio of about 0.001; and (b) a ratio of the diameter of one of the at least two particles to a width of the link is at least about 0.5 **or** the ratio of the diameter of one of the at least two particles to a width of the link is at most about 100, it is respectfully noted that *any* number would read on the instantly claimed aspect ratios when stated in the alternative. For example, with regard to the link a number such as 1001 is greater than 1000, and thus would not read on "at most 1000," but reads on "at least 0.001." Likewise, with regard to diameter of particle to width of link, a number such as 0.1 is less than 0.5 and thus would not read on "at

least 0.5," but reads on "at most about 100." Furthermore, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio within the extremely broad ranges based on the diameter of the particles as a ratio to any length available.

Applicant argues on pages 11-12 of the Response that for the reasons noted above, the combination of Jacobsen, Greene and Smith does not render the claimed subject matter unpatentable under 35 U.S.C. § 103(a), and that Mazzocchi does not cure the deficiencies of these references. Applicant argues that Mazzocchi does not even relate to embolic devices. To the contrary, Mazzocchi describes filters to remove embolic particles from a blood vessel (e.g., Mazzocchi at col. 19, lines 53-64). In particular, Mazzocchi describes resiliently expandable tubular metal fabric devices forming a bell-shaped fabric disc oriented perpendicular to the axis of the metal fabric tube. These devices are used to form a temporary filter deployed to trap embolic particles within a body channel (e.g., Mazzocchi at col. 2, line 53 - col. 3, line 29 and col. 19, lines 53-64). Mazzocchi fails to disclose or render obvious particles joined by a link having an aspect ratio of at least 0.001 or an aspect ratio of at most 1,000, where the aspect ratio is the ratio of the length of the link to the width of the link. Mazzocchi discloses an entirely different aspect ratio. Mazzocchi describes an aspect ratio of "the ratio of the length of the device over its maximum diameter or width," which is desirably at least about 1.0 and preferably about 1.0 to 3.0 (Mazzocchi at col. 11, lines 59-63,

emphasis added). Mazzocchi fails to disclose or render obvious particles joined by a link having the claimed aspect ratios. Furthermore, the Office Action does not explain where the prior art references disclose or render obvious joined particles with the ratio of the diameter of one particle to the width of a link joining the particles being at most about 100 or at least about 0.001.

This is not found to be persuasive. See for example Fig 5a and 5b and description at column 10, lines 65+ - column 11, of Mazzochi referring to a vascular occlusion device, e.g. an embolic device. The disclosure of Mazzochi is not limited to a filter. ." Furthermore, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio within the extremely broad ranges based on the diameter of the particles as a ratio to any length available.

Claims 1 – 7, 15, 17, 19, 21, 22, 25 – 31, 49 – 54 and 56 – 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobsen (US 6,530,943) in view of Mangin (WO 01/66016).

Jacobsen discloses an embolic device comprised of a linear sequence of flexibly interconnected miniature beads. The device generally comprises a flexible elongated filament having a linear sequence of beads disposed thereon. The beads may be fixedly connected to the filament. The beads may be integrally formed on the material of the filament (column 4, line 24). The string of beads may be configured to the exact

length needed. The beads may be porous (abstract). The embolic device is used to occlude blood flow and/or initiate blood clotting upon introduction to the body via a catheter (column 1, lines 14 – 25). The string of beads includes a filament (i.e. a link) and beads. The beads have diameters from 0.002 inches to 0.0018 inches, and may be made of a variety of materials, including polymers, radioopaque polymers, metals. The string of beads may be comprised of beads of several different materials (column 4, lines 25 – 40). The filament can be a multi or monofilament polymer (column 5, line 21). The string of beads may be configured as a drug delivery device, wherein the beads are porous and contain a medicament for controlled release into the interior of the body (column 2, lines 44 – 47).

Jacobsen does not specifically recite that the polymer is polyvinyl alcohol, and does not specifically recite that the porous beads have interior and surface regions wherein the mean size of pores of the interior region is greater than the mean size of pores of the surface region.

Mangin discloses embolic particles suitable for effectuating embolization or occlusion of a vessel or duct (abstract). Such particles have one or more voids on the surface and present within the particles. The particles may be a variety of sizes (see page 7, lines 18 – 35). The voids may be filled with biologically active agents or drugs page 9, line 23 – 26. The embolic particles are preferably made of PVA (page 4, line 34). The particles appear to be capable of having larger pore sizes, on average, in an "interior region" of the particle as opposed to a "surface region." See Figure B. The

examiner arbitrarily defines a "surface region" and an "interior region," as set forth in the Office Action mailed 8/23/2007.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to apply porous PVA particles, such as those taught by Mangin, in an interconnected form, as taught in the device of Jacobsen because both the porous particles of Mangin and the interconnected porous beads of Jacobsen are used for embolization. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Jacobsen specifically teaches that hydrophilic particles which are used for occluding blood flow tend to become dislodged from the target site and migrate within the body potentially causing trauma or unwanted thrombosis, and that providing a device comprising a linear sequence of interconnected miniature beads is superior to individual particles because the device is less susceptible to migration within the body (column 1 – 2). Regarding the limitations wherein the particle chain includes at least one of the following: (a) the link having an aspect ratio of at most about 1000 **or** the link having an aspect ratio of about 0.001; and (b) a ratio of the diameter of one of the at least two particles to a width of the link is at least about 0.5 **or** the ratio of the diameter of one of the at least two particles to a width of the link is at most about 100, it is respectfully noted that *any* number would read on the instantly claimed aspect ratios when stated in the alternative. For example, with regard to the link a number such as 1001 is greater than 1000, and thus would not read on "at most 1000," but reads on "at least 0.001." Likewise, with regard to diameter of particle to width of link, a number such as 0.1 is less than 0.5 and thus would not read

on "at least 0.5," but reads on "at most about 100." Furthermore, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio within the extremely broad ranges based on the diameter of the particles as a ratio to any length available.

Applicant argues on pages 12-13 of the Response that as discussed above, Jacobsen discloses a chain of particles having a central bore and a particular density. Mangin discloses unconnected embolic particles having voids present within the particles as well as on the surface of the particles, where the surface region has both large pores and small pores (e.g., Mangin, FIG. 1A), and the interior region also has both large pores and small pores (e.g., FIG. 1B). Applicant asserts that neither Jacobsen nor Mangin, either alone or in combination, discloses or renders obvious such particle chains. Applicant asserts that with regard to Figure 1 of Mangin, one of ordinary skill in the art would understand, an "interior region" of a particle is three dimensional and a "surface region" of a particle is two or three dimensional and therefore to obtain features of the surface and interior regions of a particle, more than one cross-sectional view of the particle is required, and that one would also understand that even though Mangin's Figure B shows that the two dimensional circumference includes pores having larger sizes than the pores in the two dimensional circular area, one cannot conclude that in a three dimensional space, Mangin's particle includes a surface region that has pores with larger mean sizes than the pores in the interior region of the particle. To

strictly analyze the distribution of pore sizes in Mangin's particles, infinite numbers of cross-sectional views as shown in Mangin's Figure B are needed. In fact, nowhere does Mangin disclose or otherwise indicate that his particles have an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region, as recited by the rejected claims.

This is not found to be persuasive. A single figure depicting a cross-section of a particle can be sufficient to demonstrate pore size distribution. This interpretation is supported by the instant specification, which shows only a cartoon of a single cross section, see Figure 5 of the instant Application.

Claims 1 – 4, 6, 7, 15, 17, 19 – 23, 25 – 31, 49 – 54 and 56 - 59 are rejected under 35 U.S.C. 103(a) as being obvious over Jacobsen *et al.* (US 6,530,934) in view of Lanphere *et al.* (US 2003/0185895).

Jacobsen discloses an embolic device comprised of a linear sequence of flexibly interconnected miniature beads. The device generally comprises a flexible elongated filament having a linear sequence of beads disposed thereon. The beads may be fixedly connected to the filament. The string of beads may be configured to the exact length needed. The beads may be porous (abstract). The embolic device is used to occlude blood flow and/or initiate blood clotting upon introduction to the body via a catheter (column 1, lines 14 – 25). The string of beads includes a filament (i.e. a link) and beads. The beads have diameters from 0.002 inches to 0.0018 inches, and may be

made of a variety of materials, including polymers, radioopaque polymers, metals. The string of beads may be comprised of beads of several different materials (column 4, lines 25 – 40). The filament can be a multi or monofilament polymer (column 5, line 21). The string of beads may be configured as a drug delivery device, wherein the beads are porous and contain a medicament for controlled release into the interior of the body (column 2, lines 44 – 47).

Jacobsen does not specifically recite that the porous beads have an interior and surface regions with a density of large pores, wherein the density of pores of the interior region is greater than that of the surface region.

Lanphere discloses a drug delivery device which is a substantially spherical polymer particle having an internal reservoir region including relatively large pores and a metering region substantially surrounding the reservoir region having fewer relatively large pores (paragraph 0004). A sustained, controlled-dosage release of a therapeutic agent can be achieved using the particles (paragraph 0010). The particles have a diameter in the range of 1 cm or less, e.g., 5 mm to 1 mm or less, e.g., about 1200 microns or less, and about 10 microns or more, e.g. about 400 microns or more and the pores are about 50 or 35 to 0.01 micron. Preferably, the particles are classified in size ranges of about 500-700 microns, about 700-900 microns, or about 900-1200 microns. The particles have a mean diameter in approximately the middle of the range and variance of about 20% or less, e.g. 15% or 10% or less (paragraph 0025). The particles can be used in chemoembolization (paragraph 0066). The particles are

suspended in a carrier fluid, which may include saline and a contrast solution (paragraph 0030). The particles are preferably PVA (paragraph 0021).

Lanphere fails to recite that at least two particles are connected.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize porous particles having the pore distribution disclosed by Lanphere as the porous beads in the embolic device comprised of a linear sequence of flexibly interconnected miniature beads, taught by Jacobsen, because both the embolic device of Jacobsen and the embolic particles of Lanphere are used for embolization and for controlled release drug delivery (see Jacobsen column 2, lines 44 – 47). One would have been motivated to do so because Lanphere specifically teaches that a polymeric particle having an internal reservoir region including relatively large pores and a metering region having fewer relatively large pores controls the release of an agent from the particle, and are particularly useful for delivery of desired drug dosages for an extended period of time (see Lanphere paragraphs 0003 – 0010). It would have been further obvious to one of ordinary skill in the art at the time of the instant invention to apply the porous PVA particles taught by Lanphere in an interconnected form, as taught in the device of Jacobsen, because both the porous particles of Lanphere and the interconnected porous beads of Jacobsen are used for embolization. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Jacobsen specifically teaches that hydrophilic particles which are used for occluding blood flow tend to become dislodged from the target site and migrate within the body potentially causing trauma or unwanted thrombosis, and that providing a

device comprising a linear sequence of interconnected miniature beads is superior to individual particles because the device is less susceptible to migration within the body (column 1 – 2). Regarding claims 3, 4, 6, 7 and 49 – 53, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges. Regarding the limitations wherein the particle chain includes at least one of the following: (a) the link having an aspect ratio of at most about 1000 **or** the link having an aspect ratio of about 0.001; and (b) a ratio of the diameter of one of the at least two particles to a width of the link is at least about 0.5 **or** the ratio of the diameter of one of the at least two particles to a width of the link is at most about 100, it is respectfully noted that *any* number would read on the instantly claimed aspect ratios when stated in the alternative. For example, with regard to the link a number such as 1001 is greater than 1000, and thus would not read on "at most 1000," but reads on "at least 0.001." Likewise, with regard to diameter of particle to width of link, a number such as 0.1 is less than 0.5 and thus would not read on "at least 0.5," but reads on "at most about 100." Furthermore, Jacobsen teaches that the carriers may be any desired length, and thus it would have been obvious to one of ordinary skill in the art to selectively prepare links within the claimed ranges, which would be directly related to aspect ratio within the extremely broad ranges based on the diameter of the particles as a ratio to any length available

Applicant argues on pages 13-14 of the Response that as noted above, Jacobsen describes the importance of "selecting the material of-the beads... [to] control

the density of the string" to have beads that are less than the density of blood (Jacobsen, col. 4, lines 28-32) and having a surface porosity "to promote thrombogenicity" after implantation (Jacobsen, col. 4, lines 48-53). The beads of Jacobsen are formed with a "central bore" through which a filament is "threaded to maintain the beads connected together in a chain" (Jacobsen, col. 9, line 66 - col. 10, line 1). Applicant argues that Jacobsen does not disclose or render obvious particle chain compositions where an interconnected particle has a mean pore size that is greater in a surface region than an interior region, and that Lanphere does not cure the deficiencies of Jacobsen. Applicant asserts that Lanphere discloses drug delivery particles that include a reservoir region having primarily larger pores and a metering region (e.g., Lanphere, Abstract). Jacobsen's particles in his particle chain do not include the features of Lanphere's particles. Therefore one skilled in the art would understand that Jacobsen's method of making his particle chains would not be suitable for making particle chains that include Lanphere's particles, and accordingly, one would not know how to make particle chains that include Lanphere's particles. In particular, the Office Action provides no explanation how these references, alone or in combination, describe how to:(1) place a "central bore" in each bead described by Lanphere (as disclosed by Jacobsen) and/or (2) select those particles (if any) produced by Lanphere having the pore density and surface porosity requirements described by Jacobsen. Thus, neither Jacobsen nor Lanphere, alone or in combination, discloses or renders obvious the claimed subject matter.

This is not found to be persuasive. With regard to Applicant's argument that Jacobsen emphasizes the importance of joining beads having a central bore and formed of a material having a particular density and surface porosity, Jacobsen clearly teaches that his particles can have a density which is less than that of blood (e.g. approximately 1060 kg/m^3) (column 4, line 30-31), or a density which is greater than that of blood (column 4, line 33). Therefore, Jacobsen clearly teaches a range of densities to be desirable (e.g. less than or greater than that of blood), and that density can be varied to suit a desired function. Regarding the porosity of the particles, Jacobsen does not recite any specific surface porosity, as alleged by Applicant and Smith clearly teaches porous particles. Applicant has provided no evidence to support that the properties of the particles of Smith would make them unsuitable for use as beads in the device of Johnson. Regarding the presence of a central bore, one of ordinary skill would be capable of providing such a feature, e.g. such as by skewering as taught by Greene. It is further noted that the instant claims are composition claims, not method of making claims. Furthermore, see MPEP 2145 (III) regarding arguing that prior art devices are not physically combinable. "The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference.... Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). See also *In re Sneed*, 710 F.2d 1544, 1550, 218 USPQ 385, 389 (Fed. Cir. 1983) ("[I]t is not necessary that the inventions of the references be physically combinable to render obvious the invention

under review."); and *In re Nievelt*, 482 F.2d 965, 179 USPQ 224, 226 (CCPA 1973) ("Combining the teachings of references does not involve an ability to combine their specific structures.").

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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LHS